REMARKS

Claims 29-20 and 32-37 remain pending. Favorable reconsideration is respectfully requested.

Applicants would like to thank Examiner Wehebe for the helpful and courteous discussion held with their representative on October 5, 2004. During the discussion, the outstanding rejections under 35 U.S.C. §103(a) were discussed, where the Examiner suggested submitting a Declaration to overcome the rejections. The following remarks expand on the discussion with the Examiner.

As specified in Claim 29, the present invention provides a mouse suitable as a model for atopic dermatitis, where the mouse is a NC/Nga mouse which has been sensitized with a mite extract on the ear(s) under a specific pathogen free environment, such that the animal displays at least one symptom of atopic dermatitis caused by the mite extract.

The present invention also provides a method of producing the mouse described above, and to a method of screening for an agent for effectiveness against atopic dermatitis using the mouse described above. See Claims 35 and 37, respectively.

The rejections of the claims under 35 U.S.C. §103(a) over Morita et al. in view of Yasue et al., Gad, and Hiroi et al. are respectfully traversed. Those references fail to suggest the claimed mouse, and the claimed methods of making and screening.

Applicants submit herewith an executed Rule 132 Declaration from Dr. Shozo Sakuma, an Inventor in the present application.

Dr. Sakuma has been a scientist for 24 years in the field of pharmacology and toxicology at Fujisawa Pharmaceutical Co., Ltd. in Japan. See paragraphs 1 and 2 of the Declaration.

As set forth in paragraph 6 of the Declaration, Hiroi et al., Jpn. J. Pharmacol. 76, 175-183 (1998), a copy of which is attached to the Declaration as Exhibit 5, describe using conventional NC/Nga mice to examine the effect of FK506 and steroid ointment on the development of spontaneous dermatitis. FK506 ointment (Protopic®), which is efficacious for atopic dermatitis, shows significant inhibition of spontaneous dermatitis in the NC/Nga mouse. On the other hand, commercially available betametasone valate ointment, a steroid ointment which is generally known for treating patients with atopic dermatitis, showed only a marginal effect on the development of dermatitis. See Figure 2, Figure 3 and lines 6-10 of the Abstract of Hiroi et al.

In contrast, according to Dr. Sakuma, Sasakawa et al., Int Arch Allergy Immunol 2004; 133: 55-63 (hereinafter referred to as "Sasakawa et al. I"), a copy of which is attached to the Declaration as Exhibit 6, report that both FK506 ointment and Rinderon®-V, which is the trademark for the betametasone valate ointment mentioned above, remarkably suppressed dermatitis in the mouse claimed in the above-identified application (see Figure 1 of Sasakawa et al. I).

According to Dr. Sakuma, the mice used by Sasakawa et al. I fall within the scope of Claim 29 of the present application. Sasakawa et al. state at page 56, column 2, that the mice used in the study described therein were prepared according to the procedure described in Sasakawa et al., Int Arch Allergy Immunol 2001; 126: 239-247 (hereinafter referred to as

"Sasakawa et al. II"), a copy of which is attached to the Declaration as Exhibit 7. In Dr. Sakuma's opinion, the mice produced in Sasakawa et al. II fall within the scope of Claim 29 of the present application. That this is so is demonstrated by the fact that NC/Nga mice were treated with mite extract on the ears under specific pathogen free conditions, so that the mice display symptoms of atopic dermatitis. See the last paragraph at page 2 of the Declaration.

As explained by Dr. Sakuma at the top of page 3 of the Declaration, the following table summarizes the situation with respect to treating atopic dermatitis.

	Literature Reference	Steroid Ointment	FK506 Ointment
Human Patient		○	○
Conventional NC/Nga mouse	Hiroi et al.	X	○
SPF NC/Nga mouse	Sasakawa et al. II	○	○

○: Effective

X: Ineffective

According to Dr. Sakuma, the data in the table above demonstrate that the mouse claimed in the present application, i.e., the "SPF NC/Nga mouse," can actually estimate the efficacy of Rinderon®-V, which is sold as a drug for treating atopic dermatitis. The mice described by Hiroi et al., which, as shown above, cannot be used to estimate the efficacy of Rinderon®-V, are similar to the mice described by Morita et al. These results suggest that the mouse claimed in the present application is more suitable for evaluating drug efficacy in

patients with atopic dermatitis as compared to the mouse described by Morita et al. See the paragraph under the table at page 3 of the Declaration.

Moreover, as explained by Dr. Sakuma at paragraph 7 of the Declaration, the mouse claimed in the above-identified application shows symptoms of atopic dermatitis more quickly as compared to the mouse described by Morita et al.

Dr. Sakuma also explains that Sasakawa et al. II report that the ear thickness was definitely increased from day 5-8 and the ear thickness and the severity of the skin lesions were increased with further mite antigens injections until day 18 (please refer to Figure 1 and page 242, column 1, lines 2-5 of Sasakawa et al. II). According to Dr. Sakuma, this means that the mouse claimed in the present application can be used for the screening of a new drug for atopic dermatitis only after one to three weeks from the commencement of the mite antigen injection.

In contrast, Dr. Sakuma points out the mouse described by Morita et al. would require at least 4 weeks from the commencement of applying the mite before screening could begin. Morita et al. state at page 39, under "Results," as follows:

> Four week-old mice: NC/kuj, BALB/c and C57BL/6, were kept together with mite-infested NC mice for 2 weeks to receive mites and then separated. Desquamation and crust due to scratch of skin became remarkable in NC/Kuj at 8 weeks of age.

Based on this, Dr. Sakuma explains that the mouse claimed in the present application is more suitable as a model mouse in the screening of new drug for atopic dermatitis than the mouse described by Morita et al. This is because the mouse claimed in the present application

requires a shorter amount of time for the test as compared to the mouse described by Morita et al. See paragraph 7 of the Declaration.

In Dr. Sakuma's opinion, the superior properties of the mouse claimed in the above-identified application over the mouse described by Morita et al. discussed above are unexpected from the combination of the references cited by the Examiner. See paragraph 8 of the Declaration.

According to Dr. Sakuma (please see paragraph 8 of the Declaration), Morita et al. describe the use of fur mites to induce atopic dermatitis in NC mice. The mites were not treated with the mites under a specific pathogen free environment.

Yasue et al. describe a study designed to evaluate the hyposensitizing activity of recombinant Der f 2 (rDer f 2). In the study, mice were cosensitized with rDer f 2 crude and mite extract, and then challenged with crude mite extract (see experiment 2, page 30, second column, first paragraph under the section entitled "Materials and Methods"; see also the section entitled "Experiment 2" at page 32, first column). Thus, in the procedure described by Yasue et al. the crude mite extract is administered by inhalation via an aerosol (see page 32, first column, bottom). As described at page 33, column 2, in the paragraph preceding the "Discussion" section, "inhalation of mite extract provoked late-phase airway inflammation characterized by neutrophil influx in the mice." Yasue et al. provide a detailed discussion of the biochemical responses provoked in the study described in that reference (Experiment 2, see page 33, second column, bottom to page 36). Significant by its absence is any mention of skin lesions, atopic dermatitis, or IgE.

The Gad publication is a review article describing the mouse ear swelling test (known as "MEST"). This publication provides the current version of the MEST protocol (as of 1994, when the review was published). See the Abstract. Gad fails to discuss using MEST to evaluate the effect of mite extract. Gad is also silent about using MEST to prepare a mouse model for atopic dermatitis. See paragraph 8 of the Declaration.

In Dr. Sakuma's opinion, one with those references in hand would not have been able to predict that the mouse claimed in the present application would have the properties discussed in paragraphs above. There is simply no suggestion that the mouse claimed in the present application would have those properties from the combination of Morita et al., Yasue et al. and Gad. See paragraph 8 of the Declaration.

In view of the foregoing, the claims are not obvious over Morita et al. in view of Yasue et al., Gad, and Hiroi et al. Accordingly, withdrawal of those grounds of rejection is respectfully requested.

Applicants submit that the present application is in condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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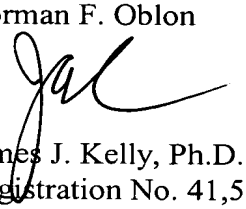
MAIER & NEUSTADT, P.C.
Norman F. Oblon



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APPENDIX

The pending claims, i.e., Claims 29, 30, and 32-37, are reproduced below.

Claims 1-28. (Canceled).

29. (Previously Amended) A mouse suitable as a model for atopic dermatitis, wherein the mouse is a NC/Nga mouse which has been sensitized with a mite extract on the ear(s) under a specific pathogen free environment, such that the animal displays at least one symptom of atopic dermatitis caused by the mite extract.

30. (Previously Amended) The mouse of Claim 29, wherein said symptom is skin lesions on the ear(s) of the mouse.

31. (Canceled).

32. (Previously Amended) The mouse of Claim 30, wherein the skin lesions are at least one member selected from the group consisting of erythema, edema, excoriation, and scaling.

33. (Previously Amended) The mouse of Claim 30, wherein the skin lesions are erythema.

34. (Previously Amended) The mouse of Claim 29, wherein the symptom is ear swelling.

35. (Previously Amended) A method of producing the mouse of Claim 29, comprising:

maintaining a NC/Nga mouse in a Specific Pathogen Free environment and sensitizing the ear(s) of the mouse with the mite extract.

36. (Previously Amended) The method of Claim 35, wherein the animal is sensitized with the mite extract for at least 5 days.

37. (Previously Amended) A method of screening for an agent for effectiveness against atopic dermatitis, comprising:

applying at least one agent to the mouse of Claim 29,

determining whether the agent reduced one or more symptoms of atopic dermatitis,

correlating a reduction in said one or more symptoms with effectiveness against atopic dermatitis, and

correlating a lack of reduction in said one or more symptoms with ineffectiveness against atopic dermatitis.